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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/729,167	12/04/2003	Patrick D. Fourney	FP0602.2 US	8624

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EXAMINER	
TELLER, ROY R	
ART UNIT	**PAPER NUMBER**
1654	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/729,167	FOURNEY ET AL.	
	Examiner	Art Unit	
	ROY TELLER	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) *32 and 33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to the action, received 2/26/08.

Claims 1-33 are pending. This application contains claims 32-33, drawn to an invention nonelected in the reply filed on 3/8/07. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 1-31 are under examination.

Response to Amendments/Arguments

Applicant's arguments and amendments filed 2/26/08 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed is herein withdrawn.

Double Patenting

Claims 1, 3-14, 16, 18, 20, 22-24, 26 and 28-31 are/stand rejected under the nonstatutory double patenting rejection for the reasons of record which are recited below.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3-14, 16, 18, 20, 22-24, 26 and 28-31 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent Application Number 10/313,643. Although, conflicting claims are not identical, they are not patentably distinct from each other because claims 1-11 of referenced non-provisional U.S. Patent Application are drawn to a method comprising the same ingredients and essentially the same steps to obtain a method as claimed in the recited claims of instant application. It would have been obvious to one of ordinary skill in the art to substitute the method for stabilizing the alpha subunit of HIF alpha in a subject of the referenced co-pending Non-provisional application with a method for regulating fat metabolism in a subject , comprising stabilizing HIG alpha in the subject, as recited in the claimed invention because said inhibitor for prolyl-4-hydroxylase also inhibits hydroxylation of hypoxia inducible factor α (i.e., HIF α).

Applicant's arguments have been carefully considered but were not found persuasive. Applicant contends that the '643 application recites methods for increasing endogenous erythropoietin and for treating an erythropoietin-associated disease, not for regulating fat metabolism or a fat metabolic process. However, the examiner contends that the '643 application is drawn to a method comprising the same ingredients and essentially the same steps to obtain a method as claimed in the recited claims of instant application. It would have been obvious to one of ordinary skill in the art to substitute the method for stabilizing the alpha subunit of HIF alpha in a subject of the referenced co-pending non-provisional application with a method for regulating fat metabolism in a subject , comprising stabilizing HIF alpha in the subject, as recited in the claimed invention because said inhibitor for prolyl-4-hydroxylase also inhibits hydroxylation of hypoxia inducible factor α (i.e., HIF α).

Claim Rejections - 35 USC § 103

Claims 1-31 are/stand rejected under 35 USC 103(a) for the reasons of record which are restated below.

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR §1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § *102*(f) or (g) prior art under 35 U.S.C.§ 103(a).

Claims 1-31 are rejected under 35 U.S.C. § 103 (a) as obvious over combined teachings from Edwards et al. USPN 5,916,898 in view of Muller (EP 0878 480).

The instant claims recite a method to stabilize the alpha subunit of hypoxia inducible factor α (i.e., HIF α) in a subject via administering to said subject a compound that inhibits hydroxylation of hypoxia inducible factor α (i.e., HIF α), therby regulating fat metabolism. Said compound is also an inhibitor for HIF prolyl hydroxylase, wherein said HIF prolyl hydroxylase is a procollage prolyl-4-hydroxylase. Claims additionally recite that said inhibitor compound is a phenanthroline and is administered to a mammal *in vivo*. Claims further recite said procollagen prolyl-4-hydroxylase enzyme is selected from a Markush group comprising EGLN1, ELN2, zEGLN3 or a combination thereof. Said HIF α is selected from a Markush group consisting of HIF-1 α, HIF-2 α , or HIF-3 α.

Edwards et al teach a pharmaceutical composition comprising phenanthrolines (e.g., 3-carboxy-4-oxo-3, 4-dihydro-1, 10-phenanthroline) said phenanthrolines (Column 14, Lines 45-67) c posseses inhibitory activity for prolyl-4-hydroxylase (Column 13, Lines 35-40). Edwards et al. further teach that said pharmaceutical compositions are administered to warm blooded animals including human (Column 14, Lines 52-54; Column 17, Lines 1-10). Edwards et al. also teach *in vitro* and *in vivo* inhibition of hydroxylation at the 4-trans position of prolyl residues within collagen in the uteri of immature female rats via subcutaneously administering the test compounds (Column 28, Example 16 d). Edwards et al. further teach that phenathrolinones are phenanthrolines that possess at least one asummytric carbon atom (See Column 13, Lines 30-35). Thus Edwards et al. explicitly and inherently teach a method to stabilize the alpha subunit of hypoxia inducible factor α in a subject via administering to said subject a compound that inhibits hydroxylation of hypoxia inducible factor α (i.e., HIF α).

Muller teaches a method to stabilize HIF alpha in an individual via injecting a compound (i.e., iron chelator a or a'-dipyridyl (i.e., DPY)) to inhibit prolyl-4- hydroxylase (Column 4, Lines 49-54; Column 9, Lines 45-48) which is manasfested as inhibiting basal membrane formation induced by a lesion of neuronal tissue. Thus, Muller intrinsically teaches that inhibiting prolyl-4-hydroxylase enzyme stabilizes HIF-alpha in an individual. Muller also teaches that said inhibitor of prolyl-4- hydroxylase to inhibit formation of basal membrane is administered locally to neuronal tissue, intraventricularly, systemically, intravenously, or orally to prevent/inhibit basal membrane formation induced by a lesion of neuronal tissue (Column 2, Line 8 to Column 11, Line 2). Note that inhibition of said enzyme would intrinsically stabilize the alpha subunit of hypoxia inducible factor (i.e., HIF alpha); because the prior art method teaches inhibition of same enzymes as is recited in instantly claimed invention. (i.e., administering a preparation that for e.g., inhibits lysyl and prolyl–4- hydroxylases enzymes) to stabilize HIF alpha. Furthermore, the prior art methods teach inhibition of said enzymes under *in vitro*, and also under *in vivo* conditions in an animal/mammal/human by administering an inhibitor for said enzyme. Note further that since HIF alpha is stabilized with an inhibitor of prolyl-4- hydroxylase, the prior art methods intrinsically teach a method to stabilize the alpha subunit of hypoxia inducible factor α (i.e., HIF α) in a subject via administering to said subject a

compound that inhibits HIF α via inhibiting inhibiting HIF α, any of the HIF α, or 2-oxoglutarate dioxygenease enzyme claimed instantly. Said subject a compound that inhibits hydroxylation of hypoxia inducible factor α (i.e., HIF α) and Muller remedies the deficiencies in teachings of Edwards et al. of actually administering said inhibitor in a human. The prior art references cited above do not enumerate the regulating of fat metabolism as claimed in the instant invention. However, adjustment of particular conventional working conditions (e.g.,the administration of HIF alpha to a subject) is deemed merely a matter of judicious selection and routine optimization of a result-effective parameter that is well within the purview of the skilled artisan.

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the teachings from Edwards et al. with those from Muller because as discussed *supra*, Muller remedies the deficiencies in Edward et al's teachings of administering said inhibitor to stabilize HIF α.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments were carefully considered but were not found persuasive. Applicant contends that Edwards neither expressly nor impliedly teaches or suggests any method for regulating fat metabolism and the deficiencies in the teachings of Edwards are not remedied by Muller. However, the examiner contends that while the prior art references cited above do not enumerate the regulating of fat metabolism as claimed in the instant invention, Edwards et al. explicitly teach a method to stabilize the alpha subunit of hypoxia inducible factor α in a subject via administering to said subject a compound that inhibits hydroxylation of hypoxia inducible factor α (i.e., HIF α). Muller intrinsically teaches that inhibiting prolyl-4-hydroxylase enzyme stabilizes HIF-alpha in an individual. Therefore, adjustment of particular conventional working conditions (e.g., the administration of HIF alpha to a subject) is deemed merely a matter of

judicious selection and routine optimization of a result-effective parameter that is well within the purview of the skilled artisan.

Claims 1-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guenzler et al. (WO 03/049686).

The instant claims recite a method to stabilize the alpha subunit of hypoxia inducible factor α (i.e., HIF α) in a subject via administering to said subject a compound that inhibits hydroxylation of hypoxia inducible factor α (i.e., HIF α), therby regulating fat metabolism. Said compound is also an inhibitor for HIF prolyl hydroxylase, wherein said HIF prolyl hydroxylase is a procollage prolyl-4-hydroxylase. Claims additionally recite that said inhibitor compound is a phenanthroline and is administered to a mammal *in vivo*. Claims further recite said procollagen prolyl-4-hydroxylase enzyme is selected from a Markush group comprising EGLN1, ELN2, zEGLN3 or a combination thereof. Said HIF α is selected from a Markush group consisting of HIF-1 α, HIF-2 α , or HIF-3 α.

Claims 1-11 of the referenced '686 application are drawn to a method comprising the same ingredients and essentially the same steps to obtain a method as claimed in the recited claims of instant application. It would have been obvious to one of ordinary skill in the art to substitute the method for stabilizing the alpha subunit of HIF alpha in a subject of the referenced application with a method for regulating fat metabolism in a subject , comprising stabilizing HIG alpha in the subject, as recited in the claimed invention because said inhibitor for prolyl-4-hydroxylase also inhibits hydroxylation of hypoxia inducible factor α (i.e., HIF α).

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments were carefully considered but were not found persuasive. Applicant contends that Guenzler neither expressly nor impliedly teaches or suggests any method for regulating fat metabolism. However, the examiner contends that claims 1-11 of the referenced '686 application are drawn to a method comprising the same ingredients and essentially the same steps to obtain a method as claimed in the recited claims of instant application. It would have been obvious to one of ordinary skill in the art to substitute the method for stabilizing the alpha subunit of HIF alpha in a subject of the referenced application with a method for regulating fat metabolism in a subject , comprising stabilizing HIG alpha in the subject, as recited in the claimed invention because said inhibitor for prolyl-4-hydroxylase also inhibits hydroxylation of hypoxia inducible factor α (i.e., HIF α).

Conclusion

All claims are rejected.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Roy Teller whose telephone number is 571-272-0971. The examiner can normally be reached on Monday-Friday from 5:30 am to 2:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RT
1654
5/19/08

/Christopher R. Tate/
Primary Examiner, Art Unit 1655